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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,915	01/05/2006	David Bryant Batt	ON?4-32701A	6407

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
BAUGHMAN, MOLLY E	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,915	BATT, DAVID BRYANT	
	Examiner	Art Unit	
	Molly E. Baughman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *4-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☒ Claim(s) *2-3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/23/05; 4/27/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group 1, Claims 1-3, and subgroup of SEQ ID NO:1-5, in the reply filed on 8/1/2007 is acknowledged.

2. Claims 4-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/1/2007.

3. Claims 1-3, and corresponding SEQ ID NO:1-5, are currently under examination.

Information Disclosure Statement

4. The information disclosure statement filed 3/23/2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

5. Claims 2-3 are objected to because of the following informalities: the claims contain non-elected subject matter, specifically, SEQ ID NO: 6-14. Appropriate correction is required.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession No. AQ264515 (i.e. Adams, 1998).

Adams of Genbank Accession. No. AQ264515 teach an oligonucleotide primer comprising SEQ ID No. 2 (see nucleotides 93-106, underlined).

It is noted while the sequence is not a primer, this is an intended use and bears no patentable weight.

8. Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession No. AV350345 (i.e. Hayashizaki, 1999).

Hayashizaki of Genbank Accession No. AV350345 teach an oligonucleotide primer comprising SEQ ID No.1 (see nucleotides 7-20, underlined).

It is noted while the sequence is not a primer, this is an intended use and bears no patentable weight.

9. Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession No. BB582522 (i.e. Hayashizaki, 2000).

Hayashizaki of Genbank Accession No. BB582522 teach an oligonucleotide primer comprising SEQ ID No.3 (see nucleotides 29-42, underlined).

It is noted while the sequence is not a primer, this is an intended use and bears no patentable weight.

10. Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession No. BE927944 (i.e. Simpson, 2000).

Simpson of Genbank Accession No. BE927944 teach an oligonucleotide primer comprising SEQ ID No.4 (see nucleotides 150-163, underlined).

It is noted while the sequence is not a primer, this is an intended use and bears no patentable weight.

11. Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession No. AA140337 (i.e. Marra, 1996).

Marra of Genbank Accession No. AA140337 teach an oligonucleotide primer comprising SEQ ID No.5 (see nucleotides 37-50, underlined).

It is noted while the sequence is not a primer, this is an intended use and bears no patentable weight.

12. Claim 3 is rejected under 35 U.S.C. 102(a or e) as being anticipated by Stratton et al. (WO 03/060111 A2).

Stratton et al. teach an oligonucleotide primer comprising SEQ ID No. 1, 2, 3, 4 or 5 (see claims 6 and 7, which *comprise* the sequences of SEQ ID No. 1, 2, 3, 4, and 5, with their corresponding mutations, and Table 1 lists the known gene sequence of the B-Raf gene with the mutation positions).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Davies et al., "Mutations of the *BRAF*-gene in human cancer," Nature, June 2002, Vol.417, pp.949-954, plus supplemental primer sequences, in view of Paranavitana, C.M., "Non-radioactive detection of K-ras mutaions by nested allele specific PCR and oligonucleotide hybridization," Mol. Cell. Probes, 1998, Vol.12, pp.309-315, or Kalinin et al., "Three novel mutations in the RET proto-oncogene," J. Mol. Med., 2001, Vol.79, pp.609-612.

Davies et al. discuss a method for detecting a specific mutation in the B-RAF gene, which comprises: (a) subjecting a segment of the B-RAF gene containing the mutation to amplification by a PCR utilizing a DNA polymerase without 3'-5' exonuclease activity (pg.953, Mutation screening) in the presence of forward and reverse primers for each exon of the B-RAF gene, wherein the second primer (i.e reverse) is complementary to a segment of the opposite DNA strand of the B-RAF gene and selected such that a detectable amplification product will be produced if the PCR occurs (see supplemental content spreadsheet containing primer sequences); and (b) detecting whether the DNA segment is amplified (see pg.953, Mutation Screening, where the resulting samples were then analyzed on a Genetic Analyzer).

Davies does not discuss the method wherein the forward primer is a detection primer, wherein the 3' end of the detection primer is complementary to a mutated base on a first DNA strand of the B-RAF gene.

Paranavitana discusses a method of analyzing a different proto-oncogene, K-*ras*, using allele-specific PCR, which comprises using a detection primer, wherein the 3' end of the detection primer is complementary to a mutated base on a first DNA strand of the B-RAF gene, along with a second primer is complementary to a segment of the opposite DNA strand of the B-RAF gene and selected such that a detectable amplification product will be produced if the PCR occurs in the presence of a DNA polymerase without 3'-5' exonuclease activity in a PCR reaction (see pg.310, Oligonucleotides and Second Step Amplification).

Kalinin et al. also demonstrate a similar method as Paranavitana to analyze another proto-oncogene, *RET*. His method also comprises detecting mutations in RET using a detection primer, wherein the 3' end of the detection primer is complementary to a mutated base on a first DNA strand of the B-RAF gene, along with a second primer is complementary to a segment of the opposite DNA strand of the B-RAF gene and selected such that a detectable amplification product will be produced if the PCR occurs in the presence of a DNA polymerase without 3'-5' exonuclease activity in a PCR reaction (pg.610, PCR amplification, SSCP analysis, and sequencing - 4th paragraph).

One of ordinary skill in the art would have been motivated to modify the method of Davies et al. to use a detection primer, wherein the 3' end of the detection primer is complementary to a mutated base on a first DNA strand of the B-RAF gene in his method to detect a specific mutation of the B-RAF gene because both Paranavitana and Kalinin demonstrate that allele-specific PCR (i.e. a method which uses a primer, with a 3' end that is complementary to a mutated base on a first DNA strand of the target gene, along with a secondary or reverse primer complementary to a segment of the opposite DNA strand of the target gene) was a conventional method in the art for detecting specific mutations of proto-oncogenes, and therefore, it would have been obvious for one of skill in the art to substitute Davies' method for the method of Paranavitana or Kalinin to achieve the predictable result of detecting a specific mutation in the B-RAF gene. The skilled artisan would have had a reasonable expectation of success in using a detection primer, wherein the 3' end of the detection primer is complementary to a mutated base on a first DNA strand of the B-RAF gene in the method of Davies et al. It

would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed detection primer therein.

15. Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Newton et al., "Analysis of any point mutation in DNA. The amplification refractory mutation system (ARMS)," Nucleic Acids Research, 1989, Vol.17, No.7, pp. 2503-2516, in view of Stratton et al. (WO 03/060111 A2).

Regarding claim 1, Newton et al. teach a method comprising comprises: (a) subjecting a segment of the B-RAF gene containing the mutation to amplification by a PCR utilizing a DNA polymerase without 3'-5' exonuclease activity in the presence of forward and reverse primers for each exon of the B-RAF gene, wherein the second primer is complementary to a segment of the opposite DNA strand of the B-RAF gene and selected such that a detectable amplification product will be produced if the PCR occurs; and (b) detecting whether the DNA segment is amplified (see pg.2504, 2nd paragraph; Figure 1; pg. 2507 - Taq Polymerase and detecting via electrophoresis; Figure 2 for primers).

Newton et al. do not discuss the method wherein mutations in the B-RAF gene are analyzed, nor wherein primers comprising SEQ ID NO: 1, 2, 3, 4, or 5 are used therein.

Stratton et al. discuss primers and methods for detecting mutations in the B-RAF gene, specifically, detecting the instant mutations which primers of SEQ ID NO:1, 2, 3, 4, and 5 detect, as disclosed in Table 1 of the specification (see pg.4-6; pg.16, 5th

paragraph; pg.17-22 Table 1 of the WO document). Stratton also disclose primers which comprise SEQ ID NO:1, 2, 3, 4, or 5 (see claims 6 and 7, which *comprise* the sequences of SEQ ID No. 1, 2, 3, 4, and 5, with their corresponding mutations, and Table 1 lists the known gene sequence of the B-Raf gene with the mutation positions).

One of ordinary skill in the art would have been motivated to modify the method of Newton et al. to use the method for detecting mutations in the B-Raf gene because Newton et al. demonstrate that such a method was conventional in the art for detecting mutations, and Stratton et al. demonstrate that the B-Raf gene, as well as the instant mutations being detected, was known in the art at the time of the invention, disclosed by Genbank Accession No. NM_004333 and noted specific mutations in Table 1. Stratton also discloses primers which comprise SEQ ID NO: 1, 2, 3, 4, and 5 and therefore, the skilled artisan would have had a reasonable expectation of success in using the primers, and detection the specific mutations of the B-RAF gene in the method of Newton et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed detection of mutations in B-RAF gene therein.

Summary

16. No claims are free of the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Molly E. Baughman whose telephone number is 571-272-4434. The examiner can normally be reached on Monday-Friday 8-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Molly E Baughman
Examiner
Art Unit 1637

MEB 9/26/07

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
9/26/07